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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,301	06/29/2001	Daniel J. Cosgrove	P04666US7	3341

27407 7590 05/22/2003

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application/No.	Applicant(s)	
09/896301	Cosgrove et al.	
Examiner	Group Art Unit	
T. Saidha	1652	13

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 3/12/03 (Paper # 12).

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 14-16, 18 & 20 ~~is~~/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 14-16, 18 & 20 ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

1. Applicant's arguments filed as per the amendment dated 3.12.03 (Paper No. 12) have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

2. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

3. Claims 14-16, 18 & 20 are under consideration in this examination.

4. The amendments filed 6.29.01 (Paper No. 6) & 3.12.02 (Paper No. 12) are objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

No method for the identification of nucleic acid comprising the method steps of claims 14-16, 18 & 20 have been described in the specification or have any basis in the specification, as originally filed. Similarly, no cDNA fragments having 70% sequence similarity to SEQ ID NO : 1 have been previously described in the specification or have any basis in the specification, as originally filed. Further, claims 18 & 20, reciting 'having greater than about 70% sequence similarity to SEQ ID NO : 2-6' or 'having greater than about 70% sequence similarity to SEQ ID NO : 2' is not described in the specification as originally filled (new).

Applicant is required to cancel the new matter in the reply to this Office Action.

Applicants' arguments :

Applicants argue that new matter is canceled in response to the office action. However, this is not the case. As indicated no method steps or/including cDNA fragments having 70% sequence similarity to SEQ ID NO : 1, are disclosed in this application as originally filed.

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Applicants indicate a new oath is being submitted separately, however, none is yet received.

6. Claims 14-16, 18 & 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 14-16, 18 & 20 are directed to a method of identifying a nucleic acid comprising 'a cDNA fragment having greater than 70% sequence similarity to SEQ ID NO : 1' (claim 14), or wherein the fragment is a 'PCR primer' or a 'hybridization probe' (Clams 15-16), or obtaining an cDNA-fragment(s) which encodes amino acid sequences having greater than about 70% sequence similarity to SEQ ID NO : 2-6 (claim 18) or designing a primer based upon 70% sequence homology to the amino acid sequence of SEQ ID NO : 2 (claim 20). The specification discloses a single cDNA

sequence (SEQ ID NO: 1) encoding cucumber cEx-29 expansin protein as the only genus. The method steps are unclear and remains undescribed. No specific cDNA-fragment(s), or hybridization conditions or amino acid modification by 30% of SEQ ID Nos. 1-7 are described. No representative number of species corresponding to polynucleotides of SEQ ID NO : 1 encoding expansin (SEQ ID Nos. 2-6) from other species and/or structure activity relationships are disclosed. There is no prior art disclosure of polynucleotide sequences encoding the catalytic polypeptides (expansin proteins) from diverse plant or animal or microorganism genera that is available in order to compare the only disclosed genus in the instant case. Claims 14-16, 18 & 20 are rejected under this section of 35 U.S.C. 112 because the claims are directed to a method of identifying a nucleic acid comprising 'a cDNA fragment ' that is 70% similar to SEQ ID NO : 1 or where the sequence is modified by 30% and no such modifications or representative number of species of polynucleotides are disclosed. A 'representative number of species' requires that the species which are expressly described be representative of the entire genus. Thus, when there is substantial variation within the genus, it may require a description of the various species which reflect the variation within the genus. In the instant case, the specification fails to describe even a single 'cDNA fragment' or 'primer' or SEQ ID NO : 1 having 70% homology to the sequence or any representative species of SEQ ID NO : 1 by structure and/or physical and chemical characteristics, representative of the entire genus which includes any catalytic polypeptide [expansin] from any source - plant, animal or microorganism, etc. What constitutes a 'representative number' is an inverse function of the predictability of the art. The number must be sufficient to identify the other members of genus. In an relatively unpredictable art,

such as the instant one, wherein the cDNA is novel but lack comparison to other related expansin cDNAs, adequate written description requirement of a genus cannot be achieved by disclosing only one species [in the sequence of SEQ ID NO : 1] within the genus. In such a case, where the members of the genus being claimed are expected to vary widely in their identifying characteristics, such as structure or activity, written description for each member within the genus will be necessary. Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

This rejection is maintained because the claimed hybridization conditions or PCR assay remain undescribed, and without such a description, or description to the 30% modification of the sequence, the written description requirement is not satisfied.

7. Claims 14-16, 18 & 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for :

'A method for identifying a nucleic acid sequence which encodes a protein with expansin activity, comprising the steps of isolating the nucleic acid sequence from a cDNA library by hybridization (under defined stringency conditions) using a DNA probe comprising the sequence of SEQ ID NO : 1',

does not reasonably provide enablement for a method of identifying a nucleic acid comprising 'a cDNA having greater than 70% sequence homology to SEQ ID NO : 1 (claim 14), or wherein the fragment is a 'PCR primer' or a 'hybridization probe' (Clams 15-16), or obtaining an cDNA-

fragment(s) which encodes amino acid sequences having greater than about 70% sequence similarity to SEQ ID NO : 2-6 (claim 18) or designing a primer based upon 70% sequence homology to the amino acid sequence of SEQ ID NO : 2 (claim 20). Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988))[*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

The claim is drawn to encompass a method of identifying a nucleic acid using 'an oligonucleotide of any size ' ..of SEQ ID NO : 1 (claim 14), or fragment of undefined size for a 'PCR primer' or a 'hybridization probe' (Clams 15-16), or obtaining cDNA-fragment(s) which encodes amino acid sequences of SEQ ID NO : 2-6 or their conservatively modified variants (claim 18) or designing a primer based upon the amino acid sequence of SEQ ID NO : 2. The specification, however, only discloses a single polynucleotide encoding a cucumber cEx-29. In addition the specification teaches the amino acid sequences (SEQ ID NO : 2 to SEQ ID NO : 5) of expansins from rice and *Arabidopsis*. Expansins are a new class of proteins that have been identified to be involved in cell wall expansion. Recent studies [Shcherban et. al, PNAS (1995, Sep 26), 92 (20) : 9245-9, not

prior art] have identified 4 distinct expansins cDNA in rice and at least 6 in Arabidopsis and show that the expansins from among these plant species, are highly conserved in size and sequence similarity (60-87 % amino acid sequence identity). Searching for sequence homology and comparison of amino acid sequence homology of expansin from Strawberry (AC : W81347), for example, and Applicants' amino acid sequence from Arabidopsis expansin (SEQ ID NO. 5) show a sequence homology of about 48.9%; and a nucleotide sequence homology of 25% between Applicants' SEQ ID NO : 1 (cucumber expansin cDNA, AC : T13320) and the nucleotide sequence of strawberry expansin (AC : V68447). Such a low nucleotide sequence homology is not always sufficient to use the Applicants' SEQ ID NO : 1 as a probe (much less for a sequence that is 70% similar to SEQ ID NO : 1 or a DNA that encodes sequences that are 70% similar to the amino acid sequences of SEQ ID NO : 2-6) in order to clone the expansin polynucleotide from strawberry, even under high stringency conditions. So, if one skilled in the art were to use a fragment of SEQ ID NO : 1 as probe in order to clone similar genes, based upon the homology factor discussed above, the chances of successful hybridization are extremely low, in view of the unpredictable nature of the art, as well as inadequate guidance [no hybridization stringency conditions are described] provided in the specification.

Thus the claims are directed to specifically encompass enormous numbers of embodiments expected to be inoperative. Since it is not routine in the art to engage in experimentation to develop method of first designing suitable polynucleotide probes which would aid in identifying other nucleic acid sequences encoding protein(s) having expansin activity, where the expectation "of success is unpredictable", the skilled artisan would require additional guidance in order to make and use the

claimed method in a manner reasonably commensurate with the scope of the claim. Without such guidance, the experimentation left to those skilled in the art is undue.

Applicants' arguments :

Applicants argue that hybridization is well known to those of ordinary skill in the art. In response it is pointed out with regard to claims 14-16, 18, directed to a method of identifying nucleotide sequence that hybridizes to a sequence which is 70% similar to the sequence of SEQ ID NO : 1, Applicants have not sufficiently defined the conditions under which the hybridizations are to take place. Nucleic acid hybridization assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. Given the unpredictability of the art and the nature of hybridization experiments in general, it is not sufficient to merely cite hybridization without a clear and explicit recitation of the conditions associated with the hybridization. For example, the definition of stringency as it pertains to hybridization conditions is subject to interpretation and is different from laboratory to laboratory. Therefore, without a clear and explicit recitation of the conditions which were actually used by Applicants in isolating the claimed polynucleotides which hybridize to the disclosed sequences, the skilled artisan would not be able to practice the claimed invention and would not be reasonably apprised of the metes and bounds of the claimed invention. Without such guidance, the experimentation left to those skilled in the art is undue.

8. No claim is allowed.

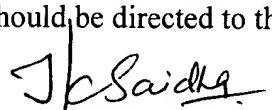
9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

a shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Tekchand Saidha
Primary Examiner, Art Unit 1652
May 21, 2003